CLAIMS

What is claimed:

1. A method for preparing an tracer composition comprising:

obtaining a ^{13}C labeled Krebs cycle metabolite precursor that will produce an analyte;

obtaining a deuterium source;

wherein gluconeogenensis is measured from a subject that was provided the precursor and the deuterium source, and produced the analyte, by comparison of the relative nuclear magnetic resonance profiles of the labeled components in the analyte.

2. The method of claim 1, wherein the analyte is ^{13}C-glucose.

3. The method of claim 1, wherein the presursor is glucose, lactose, lactate or alanine.

4. The method of claim 1, wherein the deuterium source is deuterated water.

5. The method of claim 1, wherein the analyte is glucose deuterated in the 2, 5 and 6 positions, and any

transformation that maintains the 2,5 and 6 positions in relation to one another.

6. The method of claim 1, wherein the analyte is (1-6 $^{13}C_2$)-glucose.

7. The method of claim 1, wherein the water is D_2O.

8. The method of claim 1, wherein the flux is measured from blood, urine or tissue extracts.

9. The method of claim 1, wherein the analyte is ^{13}C-labeled glucose with the label at the 2 or 5 positions, or at both positions.

10. The method of claim 9, wherein the metabolite is a transformation of the labeled glucose containing the labeled 2 position, or the labeled 5 position, or both.

11. The method of claim 1, further comprising the step of adding $^{13}C_3$-propionate.

12. The method of claim 1, wherein the Krebs cycle precursor is selected from the group consisting of pyruvic acid, acetic acid, acetoacetic acid, beta-

hydroxybutyric acid, a Krebs cycle pathway metabolite, and mixtures thereof.

13. The method of claim 1, wherein the analyte is selected from the group consisting of pyruvic acid, acetic acid citric acid, isocitric acid, cis-aconitic acid, 2-ketoglutaric acid, succinic acid, fumaric acid, malic acid, oxaloacetic acid, and mixtures thereof.

14. A method for preparing an tracer composition comprising:

obtaining a deuterium source;

wherein gluconeogenensis is measured from a subject that was provided the deuterium source, and produced an analyte, by comparison of the relative nuclear magnetic resonance profiles of the deuterium components in the analyte.

15. The method of claim 14, wherein the deuterium source is deuterated water.

16. The method of claim 14, wherein the analyte is glucose deuterated in the 2, 5 and 6 positions, and any transformation that maintains the 2,5 and 6 positions in relation to one another.

17. The method of claim 14, wherein the analyte is (1-6 $^{13}C_2$)-glucose.

18. The method of claim 14, wherein the flux is measured from blood, urine or tissue extracts.

19. The method of claim 14, wherein the analyte is selected from the group consisting of pyruvic acid, acetic acid citric acid, isocitric acid, cis-aconitic acid, 2-ketoglutaric acid, succinic acid, fumaric acid, malic acid, oxaloacetic acid, and mixtures thereof.

20. A method for preparing an isotopic metabolic flux tracer composition comprising:

providing a ^{13}C labeled Krebs cycle metabolite precursor to a subject to prouce an analyte;

obtaining a sample from the subject; and

measuring the nuclear magnetic resonance of the labeled tracers to determine the rate of gluconeogenesis.

21. The method of claim 20, wherein the analyte is ^{13}C-glucose.

22. The method of claim 20, wherein the analyte is glucose labeled with ^{13}C at positions 1 through 6, or combinations of two or more at any position.

23. The method of claim 20, wherein the analyte is (1-6 $^{13}C_2$)-glucose.

24. The method of claim 20, wherein the sample is from blood, urine or tissue extracts.

25. The method of claim 20, further comprising the step of providing the subject with $^{13}C_3$-propionate.

26. The method of claim 20, wherein the Krebs cycle precursor is selected from the group consisting of pyruvic acid, acetic acid, acetoacetic acid, beta-hydroxybutyric acid, a Krebs cycle pathway metabolite, and mixtures thereof.

27. The method of claim 20, wherein the analyte is selected from the group consisting of pyruvic acid, acetic acid citric acid, isocitric acid, cis-aconitic acid, 2-ketoglutaric acid, succinic acid, fumaric acid, malic acid, oxaloacetic acid, and mixtures thereof.

28. The method of claim 20, wherein the ^{13}C Krebs cycle precursor is provided orally.

29. A method for measuring metabolic flux in a sample using an isotopic metabolic flux tracer composition comprising:

providing the sample with a ^{13}C Krebs cycle precursor, D_2O and acetaminophen;

obtaining an analyte from the sample; and

measuring the relative amounts of acetaminophen glucuronide and phenylacetylglutamine in the analyte using nuclear magnetic resonance.

30. The method of claim 29, wherein the precursor is ^{13}C-glucose.

31. The method of claim 29, wherein the precursor is glucose labeled with ^{13}C at positions 1 through 6, or combinations of two or more at any position.

32. The method of claim 29, wherein the precursor is (1-6 $^{13}C_2$)-glucose.

33. The method of claim 29, wherein the sample is from blood, urine or tissue extracts.

34. The method of claim 29, further comprising the step of providing the subject with $^{13}C_3$-propionate.

35. The method of claim 29, wherein the Krebs cycle precursor is selected from the group consisting of pyruvic acid, acetic acid, acetoacetic acid, beta-hydroxybutyric acid, a Krebs cycle pathway metabolite, and mixtures thereof.

36. The method of claim 29, wherein the Krebs cycle precursor is selected from the group consisting of pyruvic acid, acetic acid citric acid, isocitric acid, cis-aconitic acid, 2-ketoglutaric acid, succinic acid, fumaric acid, malic acid, oxaloacetic acid, and mixtures thereof.

37. The method of claim 29, wherein the ^{13}C Krebs cycle precursor and D_2O are provided orally.

38. The method of claim 29, wherein the ^{13}C Krebs cycle precursor and D_2O are provided to a mammal.

39. The method of claim 29, wherein the ^{13}C Krebs cycle precursor and D_2O are provided to a human.

40. A reagent kit for use in effecting a simultaneous assay for gluconeogenesis in a sample, said reagent kit comprising:
a ^{13}C labeled Krebs cycle precusor; and
a labeled water tracer.

41. The reagents of claim 40, wherein the Krebs cycle precursor is ^{13}C-glucose.

42. The reagents of claim 40, wherein the Krebs cycle precursor is (1-6 $^{13}C_2$)-glucose.

43. The method of claim 40, wherein the Krebs cycle precursor is glucose labeled with ^{13}C at positions 1 through 6, or combinations of two or more at any position.

44. The reagents of claim 40, wherein the water tracer is D_2O.

45. The reagents of claim 40, wherein the Krebs cycle precursor is $^{13}C_2$-labeled glucose.

46. The reagents of claim 40, further comprising $^{13}C_3$-propionate.

47. The reagents of claim 40, further comprising acetaminophen.

48. The reagents of claim 40, further comprising an acetaminophen glucuronide and/or an phenylacetylglutamine standard.

49. The reagents of claim 40, wherein compositions are prepared for oral administration.

50. The reagents of claim 40, wherein the Krebs cycle precursor is selected from the group consisting of pyruvic acid, acetic acid, acetoacetic acid, beta-hydroxybutyric acid, a Krebs cycle pathway metabolite, and mixtures thereof.

51. The reagents of claim 40, wherein the pH of the components of the reagent kit is from about 3 to about 7.

52. The reagent kit of claim 40, further comprising a buffered isotonic solution.

53. The reagent kit of claim 40, further comprising a buffered isotonic solution wherein the buffer comprises sodium borate and potassium cyanide.

54. A method for determining gluconeogenesis comprising the steps of:

providing a patient with a ^{13}C labeled Krebs cycle precursor and D_2O;

obtaining a sample a blood, urine or tissue sample from the patient;

measuring the ^{2}H signal nuclear magnetic resonance spectra;

measuring the ^{1}H NMR nuclear magnetic resonance spectra;

measuring the ^{13}C-carbon nuclear magnetic resonance spectra; and

calculating the rate of gluconeogenesis by taking the known infusion rate of a ^{13}C radiolabelled Krebs cycle

metabolite divided by the average fraction found in the sample over a predetermined period.

55. The method of claim 54, therein the predetermined time period is between about 2 to between about 3 hours.

56. The method of claim 54, therein the predetermined time period comprises measurements at 120, 150 and 180 minutes.

57. The method of claim 54, wherein the patient fasts for 6-8 hours before taking the ^{13}C labeled Krebs cycle precursor and D_2O.

58. The method of claim 54, wherein the patient is further provided with ^{13}C propionate.